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Original article

Epidemiological characterization of the intermittent and persistent types of allergic rhinitis

Background: A new classification of allergic rhinitis (AR) has been proposed by the allergic rhinitis and its impact on asthma (ARIA) workgroup. The validity of this new classification is still largely unknown, especially the extent to which it differs from the classical seasonal/perennial (SAR/PAR) classification, and how and whether intermittent and persistent types of AR, as defined by ARIA, differ from each other.
Methods: Two-step cross-sectional, population-based, in six Western Europe countries; telephone interview followed by clinical diagnosis [including specific immunoglobulin E (IgE) measurements] in a selected subset.
Results: Within the population with AR, 29% of the subjects had persistent AR. There was no association between the intermittent/persistent and the SAR/PAR classifications. Subjects with persistent AR had more severe symptoms, and higher rate of self-awareness and previous diagnosis of AR; they were also clearly distinct in their sensitization pattern and medication use.
Conclusions: The classic types of SAR/PAR cannot be used interchangeably with the new classification of intermittent/persistent, as they do not represent the same stratum of disease. There is also evidence that the persistent type describes a distinct group with characteristics that differentiates them from intermittent AR. These results support the validity of the new ARIA classification.

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Key words: allergic rhinitis and its impact on asthma; epidemiology; intermittent allergic rhinitis; persistent allergic rhinitis.

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Allergic rhinitis (AR) is an upper respiratory disorder affecting between 10 and 40% of the global population (1). Epidemiological evidence suggests that the prevalence has been rising (2). Although AR occurs frequently, affecting both adults and children, it remains largely undiagnosed. The condition may be frequently trivialized (by the patient) and/or unrecognized (by the doctor), resulting in inadequate control of symptoms. In the UK, only 18% of subjects with rhinitis had visited their general practitioner over the preceding 2 years concerning their hay fever (3). A recent study in France showed that 19% of 230 patients with typical symptoms of AR had never consulted a doctor for their nasal problem (4). The social and economic costs incurred by this disease are substantial, contributing to increased impairment of daily activities, quality of sleep, and productivity (5).

The main symptoms of AR are sneezing, runny nose, itching, rhinorrhea, and/or nasal congestion (1). The condition was generally classified according to the suspected cause of the condition, and the time of year it occurs. The classic types were seasonal allergic rhinitis (SAR), also known as hay fever, and perennial allergic rhinitis (PAR). Described extensively in the epidemiological literature, SAR was associated with outdoor allergens such as pollen and moulds, and generally occurred during the seasons with high pollen count. The PAR was associated with indoor allergens such as dust mites, moulds, cockroaches and animal danders and could occur throughout the year at different seasons. This classification while useful, posed several problems. People allergic to several pollens may present with symptoms over several seasons while people with PAR may experience symptoms for short but recurring periods. Additionally, people who experience PAR may also suffer from seasonal exacerbations. In response to this, the Allergic Rhinitis and its Impact on Asthma (ARIA) group in conjunction with the World Health Organization (WHO), has revised the classification of AR. The new classification includes a measurement of the frequency and duration of the symptoms (1). Intermittent AR is defined as experiencing symptoms for <4 days/week or <4 consecutive weeks. Persistent AR is termed as symptoms occurring for more than 4 days/week and more than 4 consecutive weeks. Additionally, a severity scale of mild to moderate-severe was included in the revised classification.

While the SAR/PAR classification was deemed inadequate, the validity of the new classification is still largely unknown, especially the extent to which it differs from the classical SAR/PAR classification, and how and whether intermittent and persistent, as defined by ARIA, differ

from each other. In a recent study in France, Demoly et al. (6) assessed the characteristics of patients presenting for AR during the spring season (SAR) and patients presenting during the fall-winter season (PAR). Their results show that SAR was not synonymous with the ARIA intermittent type and PAR was not synonymous with the ARIA persistent type (6). While this study provides a valuable indication of the validity of the classification, it is limited in that the data were gathered in a single country, and only from patients who presented to doctors. It would be of interest to compare the classifications among subjects from the general population, possibly previously undiagnosed, and in a wider geographic area.

The present study has several aims. First, to compare the proportions of the classical and the ARIA types of AR in a population-based study (7); secondly, to describe the characteristics of both the intermittent and persistent groups, including differences or similarities in demography, severity of the symptoms, self-awareness, diagnosis rate, medication use, and sensitization patterns.

Methodology

The study was cross-sectional, population-based, and was conducted in six countries in Western Europe (Belgium, France, Germany, Italy, Spain, UK). It was designed to include samples as representative of the general population as possible and to have the ability to identify previously undiagnosed cases. There were two consecutive, integrated steps. In step 1, telephone numbers were randomly selected to conduct telephone interviews of the general population age 18 or more. A questionnaire was administered to measure the prevalence of AR and to screen potential subjects with AR, based on symptoms or self-awareness; this screening was designed to be highly sensitive (and could therefore not be highly specific). Subjects with symptoms were also asked to provide information on the frequency and duration of these symptoms in terms of number of days and number of consecutive weeks. They were not aware of the possible use of the answers for a new disease classification. The classification into persistent (if their symptoms lasted ≥4 days/week and ≥4 consecutive weeks) or intermittent (if otherwise) was added to the database after completion of the study.

The 20-items questionnaire for the telephone interview had the following structure:

- presence of nasal and eye symptoms;
- indoor/outdoor triggers;
- self-awareness of AR, including previous medical diagnosis;
- disease duration;
- medication (yes/no);
- symptoms: time of year, days per week and number of weeks;
- smoking status; and
- demography, occupation, education level

All subjects who screened positive for AR at study step 1 were invited to one of 26 participating clinical centres for a physical examination and blood sampling, and to complete a questionnaire. Doctors were instructed to establish a diagnosis according to their usual practice including the SAR/PAR classification of patients; patients with both SAR and PAR were classified as PAR. Specific immunoglobulin E (IgE) measurements (Pharmacia CAP system, Uppsala, Sweden) were taken for six groups of allergens: grass, tree and weed pollens, animal danders, moulds and dust mite. For grass, tree and weed pollens the investigator was instructed to select one among a panel of three to five tests, according to local pollens. All six tests were a mix of several allergens, except for Olive tree and *Parietaria*, which were offered as an option in the panel for tree and weed pollen, respectively. For the present analyses, subjects were considered as sensitized to a given group of allergens if the measurement of IgE was equal to or above 0.35 kU/l. Frequency and severity of specific symptoms (runny nose, blocked nose, itchy nose, sneezing, itchy or watery eyes, and poor quality of sleep were assessed) on a 4-point verbal descriptor scale (frequency: 0 = never, 1 = rarely, 2 = quite often, 3 = very often; severity: 0 = no problem; 1 = problem present but not disturbing; 2 = disturbing problem but not hampering any activity or sleep; 3 = problem hampering some activities or sleep). Mean total scores for all symptoms were also calculated.

Univariate comparisons of two samples were performed by Wilcoxon–Mann–Whitney test or chi-square test of contingency. The hypothesis of independence between the two classifications of AR was tested by a chi-square test of contingency in a 2×2 table. Additional description of the study can be found in Ref. (7).

Ethics

Approval was obtained from the Ethics or Scientific Committee in each country and study centre. All subjects participating in step 2 had signed an informed consent.

Results

There were a total of 9646 telephone interviews (study step 1). The median age of the subjects was 44 years; there were 54% women; further details are described in Ref. (7). Subjects who self-identified as having AR numbered 19% of the population, and of this group, 70% reported having a doctor diagnosis of AR. Among those who self-identified as having AR, 70% were intermittent, 30% persistent; among those with previous diagnosis of AR, 67% were intermittent, 33% persistent. The proportion of SAR was 49% (51% PAR; among those with previous diagnosis of AR).

A total of 726 subjects completed step 2 by attending a clinical centre. The investigators diagnosed AR in 411 (57%) subjects. Of this group, 55% had been previously diagnosed with AR while 45% had not received any such diagnosis. Subjects with clinically confirmed AR were further grouped into ARIA types based on the frequency and duration of symptoms assessed at step 1. Here, 71% were identified as intermittent and 29% were identified as persistent. Additionally, during the visit to the centre, clinicians grouped subjects into the classic AR designations; 49% were SAR while 51% were PAR. When the two classifications are cross-tabulated, it appears that approximately half of the persistent were SAR, and half of the intermittent were PAR (Table 1). The null hypothesis that the two classifications are independent was tested and could not be rejected ($\chi^2 = 0.66$, d.f. = 1, $P = 0.42$), meaning that being SAR or PAR was not predictive of being intermittent or persistent.

Table 1. Cross-tabulation of ARIA and SAR/PAR classifications ($N = 401$)

	Intermittent	Persistent
SAR ($N = 193$)	133	60
PAR ($N = 208$)	151	57

Due to missing value on either one of the two classifications, 10 subjects (2.4%) are excluded from this table.
ARIA, allergic rhinitis and its impact on asthma; SAR, seasonal allergic rhinitis; PAR, perennial allergic rhinitis.

Table 2. Comparison of subjects with intermittent or persistent allergic rhinitis (AR)

	Intermittent (%)	Persistent (%)	*P*-value for no difference between groups
Age (median)	35	36	0.50
Gender (% men)	52	54	0.78
Self-awareness of AR	63	83	<0.0001
Previous diagnosis	49	66	0.002
Self-reported asthma	21	20	0.93

Table 3. Comparison of mean score of frequency and severity of symptoms

	Intermittent ($N = 287$)	Persistent ($N = 119$)	*P*-value for no difference between groups
Symptom frequency (scale 0–3)			
Mean score runny nose	1.78	2.04	0.001
Mean score blocked nose	1.73	2.01	0.003
Mean score itchy nose	1.64	1.87	0.02
Mean score sneezing	1.92	1.99	0.41
Mean score itchy or watery eyes	1.55	1.82	0.003
Mean score poor quality sleep	0.93	1.25	0.005
Symptom severity (scale 0–3)			
Mean score runny nose	1.43	1.74	0.001
Mean score blocked nose	1.63	1.83	0.093
Mean score itchy nose	1.12	1.26	0.14
Mean score sneezing	1.43	1.63	0.05
Mean score itchy or watery eyes	1.30	1.73	0.0002
Mean total score	6.94	8.22	0.0005

The comparisons of intermittent and persistent subjects for median age, gender, symptom severity, self-awareness of AR, previous diagnosis, and self-reported asthma are in Table 2. No difference was found for age, gender or self-reported asthma. There was, however, greater self-awareness of AR among the persistent group, 83% *vs* 63%, and a larger proportion of the persistent group had had a previous diagnosis. Table 3 shows that not only the frequency but also the severity of the five symptoms measured were higher among the persistent group than among the intermittent. The total severity mean scores of 8.2 *vs* 6.9 show a higher severity among the persistent group compared with the intermittent group.

Table 4. Comparison of medication use for subjects with intermittent or persistent allergic rhinitis (AR)

	Intermittent (%)	Persistent (%)	*P*-value for no difference between groups
Ever seen doctor about nasal problems	64	83	0.0003
Prescription for nose problems	58	81	<0.0001
Medication use			
N	174	82	
Everyday throughout the year	4.6	12.2	
Everyday during the period with symptoms	35.6	50.0	0.002
Only on the specific days, when necessary	59.8	37.8	

Table 5. Comparison of allergen-specific sensitization (immunoglobulin E, IgE) for subjects with intermittent or persistent allergic rhinitis (AR) ($N = 405$)

Allergen-specific sensitization	Intermittent (%)	Persistent (%)	*P*-value for no difference between groups
Grass pollen	48.3	63.0	0.007
Tree pollen	29.4	40.3	0.03
Weed pollen	24.5	32.8	0.08
Moulds	11.9	5.9	0.07
Animal danders	25.9	25.2	0.89
House dust mites	52.4	41.3	0.04

More subjects with persistent AR had previously seen a doctor about nasal problems and rate of doctor prescribed medication was higher for the persistent group (Table 4). Half of the subjects with persistent disease used medication every day, while on the other hand, the majority of subjects with intermittent disease used medication as needed (Table 4). Sensitizations to tree, grass pollen and dust mites were significantly different between the groups (Table 5). Subjects with persistent AR were relatively more often sensitized to pollens, but less often to house dust mites.

Discussion

In this large cross-sectional study, we addressed several questions about the new ARIA definition. We found the proportions for intermittent/persistent and SAR/PAR to be quite consistent in the two populations, i.e. subjects reporting a previous diagnosis AR (study step 1) and subjects with clinically confirmed diagnosis of AR and possibly previously undiagnosed (step 2): in both cases persistent AR represented about one-third of the population with AR, while the division into SAR/PAR was close to 50 : 50%. The relative frequency of the two new ARIA types between SAR and PAR subjects was also addressed. Results similar to that of the Demoly et al. study (6), based on patients visiting their doctors, were found, in that a large proportion of those classified as

SAR experienced persistent disease, and a large proportion of the PAR experienced intermittent disease. A statistical comparison of the two classifications showed that they were independent and cannot be used interchangeably.

The results show that subjects with persistent AR experienced higher discomfort prior to the study to seek medical attention for their condition more often. They had also more medication prescribed for them by the doctors, and were using medication in a pattern different from the subjects with intermittent AR. This, coupled with the higher mean scores for symptom frequency and higher severity found in the persistent group confirms that a sizeable part of the population experience chronic disability because of persistent AR. This population will probably need specific treatment management, as indicated in the ARIA guidelines (1, 8). Specific studies focused on this group of patients will answer these questions (9). A recent study in five Western European countries tested the effect of treatment in persistent AR; this study showed that when patients suffering from persistent rhinitis received long-term therapy, the treatment group showed a benefit, in terms of both quality of life and a decrease in disease burden over that of the placebo group (10).

In conclusion, the classic types of SAR/PAR cannot be used interchangeably with the new classification of intermittent/persistent, as they do not represent the same stratum of disease. There is also evidence that the persistent AR classification describes a distinct group with characteristics that differentiates them from intermittent AR and upholds the ARIA classification.

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